

CLAIMS

What is claimed is:

1. A method of detecting a target nucleic acid sequence,
5 comprising:
 providing a hybridization complex comprising (a) a capture probe that
 is attached to a solid surface and (b) a target nucleic acid sequence that is
 hybridized to the capture probe, wherein the target nucleic acid sequence
 additionally comprises at least one nanoparticle attached to the target
10 nucleic acid sequence;
 exposing the solid surface to light at a wavelength absorbed by the
 nanoparticle; and
 detecting a temperature of the solid surface, whereby detection of an
 increased temperature relative to a temperature of the solid surface that
15 would be detected in the absence of said complex indicates the presence or
 amount of target nucleic acid sequence hybridized to the solid surface.
2. The method according to claim 1, comprising:
 hybridizing a target sequence to at least one capture probe to form a
20 first hybridization complex, wherein the capture probe is attached to a solid
 surface;
 hybridizing a detection probe to the first hybridization complex to form
 a second hybridization complex, wherein the detection probe comprises a
 nanoparticle;
25 exposing the solid surface to light at a wavelength absorbed by the
 nanoparticle; and
 detecting the temperature of the solid surface at the attachment
 location of the capture probe, wherein an increase in temperature at the
 attachment location as compared to the background temperature of the solid
30 surface indicates hybridization of the target sequence to the solid surface.
3. The method of Claim 1, wherein the target sequence
 comprises RNA.

4. The method of Claim 1, wherein the target sequence comprises cDNA.

5 5. The method according to Claim 1, wherein the solid surface comprises indium tin oxide.

6. The method according to Claim 1, wherein the target sequence is present in a biological sample.

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7. The method according to Claim 2, wherein the detection probe comprises a nanoparticle comprising one or more of metals and metal oxides.

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8. The method according to Claim 7, wherein the nanoparticle comprises a metal comprising one or more of gold, silver, and platinum.

9. The method according to Claim 1, wherein the nanoparticle comprises gold.

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10. The method according to Claim 1, wherein the nanoparticle is a nanoshell.

11. The method according to Claim 1, wherein the nanoparticle has a diameter from about 10 to about 20 nanometers.

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12. The method according to Claim 1, wherein the nanoparticle exhibits surface plasmon resonance, and wherein the solid surface is exposed to light at a wavelength that matches the surface plasmon resonance of the nanoparticle.

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13. The method according to Claim 1, wherein the light is generated by a laser.

14. The method according to Claim 2, wherein the detection probe further comprises an oligonucleotide attached to the nanoparticle.

5 15. The method according to Claim 14, wherein the capture probe is complementary to a first target domain of the target sequence, and the detection probe oligonucleotide is complementary to a second target domain of the target sequence.

10 16. The method according to Claim 2, wherein the detection probe comprises a nanoparticle attached to one partner of a ligand-binding pair, and the target sequence comprises the other partner of a ligand-binding pair.

15 17. The method according to Claim 16, wherein one partner of a ligand-binding pair is streptavidin, and the other partner of the ligand-binding pair is biotin.

 18. The method according to Claim 16, wherein the target sequence comprises biotin.

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 19. The method according to claim 18, wherein the biotin has been incorporated into the target sequence during nucleic acid amplification.

25 20. The method according to Claim 18, wherein the detection probe comprises a nanoparticle attached to streptavidin.

 21. The method according to Claim 1, wherein a plurality of different capture probes are attached to the solid surface in an array, and the location of each capture probe comprises an array element.

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 22. The method according to Claim 21, wherein each array element is exposed to light separately.

23. The method according to Claim 21, wherein the entire plurality of capture probes is exposed to light simultaneously.

24. The method according to Claim 1, wherein the light is provided
5 by a light source is selected from the group consisting of a tungsten halogen light source, a xenon arc lamp and a laser.

25. The method according to Claim 1, where in the exposing is by
rastering.
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26. The method according to Claim 1, wherein the target sequence is selected from the group consisting of an mRNA sequence derived from a sample and a cDNA sequence derived from a sample.

27. The method according to Claim 1, wherein the capture probe
15 comprises a sequence from a gene of interest.

28. The method according to Claim 1, wherein the capture probe comprises or is suspected to comprise a mutation to be detected
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29. The method according to Claim 1, wherein the target sequence comprises or is suspected to comprise a mutation to be detected

30. The method according to Claim 1, wherein the nanoparticle
25 comprises silver and the solid surface is exposed to light at a wavelength ranging from about 420-460 nm.

31. The method according to Claim 1, wherein the nanoparticle comprises gold and the solid surface is exposed to light at a wavelength of
30 about 532 nm.

32. The method according to Claim 1, wherein the detecting step is carried out by a thermocouple attached to a side of the solid surface upon which capture probes are not attached.

5 33. The method according to Claim 1, wherein the detecting step is carried out by infrared thermography.

34. The method according to Claim 1, wherein the detecting step is carried out by Fourier Transform infrared thermography.

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35. The method according to Claim 1, wherein the detecting step comprises capturing a thermal image by means of an infrared camera.

15 36. The method according to Claim 1, wherein the detecting step is carried out by a charge coupled device.

37. The method according to claim 1, wherein the nanoparticle is attached to the target sequence.

20 38. The method according to claim 37, where the nanoparticle is attached to the target sequence by one of a binding pair and complementary nucleic acids.

25 39. The method according to claim 37, where the nanoparticle is attached to the target sequence by one of primer extension and ligation of a nanoparticle-labeled nucleic acid.

40. The method of claim 1, wherein the complex comprises a detection probe.

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41. The method of claim 40, wherein the detection probe is attached to the target sequence before, during, or after the target sequence hybridizes to the capture probe.

42. The method of claim 40, comprising the sequential steps of hybridizing the target to the capture probe; and then reacting the hybrid with a detection probe.

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